FGF9-Pitx2-FGF10 signaling controls cecal formation in mice.

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Public Summary:
Fibroblast growth factor (FGF) signaling to the epithelium and mesenchyme mediated by FGF10 and FGF9, respectively, controls cecal formation during embryonic development. In particular, mesenchymal FGF10 signals to the epithelium via FGFR2b to induce epithelial cecal progenitor cell proliferation. Yet the precise upstream mechanisms controlling mesenchymal FGF10 signaling are unknown. Complete deletion of Fgf9 as well as of Pitx2, a gene encoding a homeobox transcription factor, both lead to cecal agenesis. Herein, we used mouse genetic approaches to determine the precise contribution of the epithelium and/or mesenchyme tissue compartments in this process. Using tissue compartment specific Fgf9 versus Pitx2 loss of function approaches in the gut epithelium and/or mesenchyme, we determined that FGF9 signals to the mesenchyme via Pitx2 to induce mesenchymal Fgf10 expression, which in turn leads to epithelial cecal bud formation.

Scientific Abstract:
Fibroblast growth factor (FGF) signaling to the epithelium and mesenchyme mediated by FGF10 and FGF9, respectively, controls cecal formation during embryonic development. In particular, mesenchymal FGF10 signals to the epithelium via FGFR2b to induce epithelial cecal progenitor cell proliferation. Yet the precise upstream mechanisms controlling mesenchymal FGF10 signaling are unknown. Complete deletion of Fgf9 as well as of Pitx2, a gene encoding a homeobox transcription factor, both lead to cecal agenesis. Herein, we used mouse genetic approaches to determine the precise contribution of the epithelium and/or mesenchyme tissue compartments in this process. Using tissue compartment specific Fgf9 versus Pitx2 loss of function approaches in the gut epithelium and/or mesenchyme, we determined that FGF9 signals to the mesenchyme via Pitx2 to induce mesenchymal Fgf10 expression, which in turn leads to epithelial cecal bud formation.